

Serial No. 10/032,238

Docket No. 0075.00

REMARKS**I. Introductory Comments**

In the Office Action under reply, the Examiner has maintained and made final the requirement for restriction between Groups I, II, and III. In addition, the Examiner rejected the claims as follows: under 35 U.S.C. §112, second paragraph, for alleged indefiniteness (claims 1-40); under 35 U.S.C. §102(b) as allegedly being anticipated Nossal (claims 1-32 and 37-40); under 35 U.S.C. §103(a) as allegedly being unpatentable over Mosley *et al.* (U.S. Patent No. 5,599,905) in view of Platz *et al.* (U.S. Patent No. 6,582,728) (claims 1-40); and under 35 U.S.C. §103(a) as allegedly being unpatentable over Lange in view of Platz *et al.* (U.S. Patent No. 6,582,728) (claims 1-40). The rejections are traversed for reasons provided below.

II. Amendments to the Specification and Claims**A. Specification**

The specification has been amended to correct matters relating to form, as follows.

In the paragraph appearing on page 3, beginning at line 3, the words "other" and "be", and the commas (",") appearing before and after the word "thus" have been deleted.

In the paragraph appearing on page 3, beginning at line 17, a comma (",") has been deleted on lines 4 and 10 of the paragraph.

In the paragraph appearing on page 5, beginning at line 16, "IL-4" has been changed to read -- IL-4R --.

In the paragraph appearing on page 6, beginning at line 12, each of "IL4R" and "IL-4" has been changed to read -- IL-4R --.

In the paragraph appearing on page 7, beginning at line 23, "sIL'4R" has been changed to read -- sIL-4R --.

In the paragraph appearing on page 8, beginning at line 5, the conjunction -- , or -- has been added to the second line of this paragraph.

In the paragraph appearing on page 11, beginning at line 21, the spelling of the word "includes" has been corrected.

In the paragraph appearing on page 12, beginning at line 26, the word "chance" has been changed to the word -- change --.

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In the heading appearing on page 13, line 7, capitalization of the word "Powder" has been effected.

In the paragraph appearing on page 13, beginning at line 17, the word "condition" has been changed to -- conditions -- and the word -- surprising -- has been changed to the word -- surprisingly --.

In the paragraph appearing on page 14, beginning at line 3, the word -- shows -- has been added to the ninth line of this paragraph.

In the paragraph appearing on page 16, beginning at line 21, "II-4R" has been changed to read -- ~~II-4R~~ --.

In the paragraph appearing on page 16, beginning at line 27, "II-4R" has been changed to read -- ~~II-4R~~ --.

In the paragraph appearing on page 17, beginning at line 22, the spelling of the word "polypeptides" has been corrected and the capitalization of the word "International" has been effected.

In the paragraph appearing on page 17, beginning at line 28, the word "peptide" has been changed to -- peptides --, the incorrect abbreviation "(try)" has been changed to -- (tyr) --, the spelling of the word "histidine" has been corrected, and the numeral "2" has been written out.

In the paragraph appearing on page 18, beginning at line 27, the spelling of the word "fructose" has been corrected, the conjunction "a nd" has been corrected to read as -- and --, and a space has been inserted between "as" and "mannitol"

In the paragraph appearing on page 19, beginning at line 6, "suchas" has been corrected to read -- such as --, the spelling of the word -- polymeric -- has been corrected, the spelling of the word "sorbitan" has been corrected, the word "may" has been deleted, and a space has been added before the word "or."

In the paragraph appearing on page 19, beginning at line 21, the year has been corrected to include only four digits.

In the paragraph appearing on page 20, beginning at line 11, "II-4R" has been changed to read -- ~~II-4R~~ --.

In the paragraph appearing on page 21, beginning at line 15, the spelling of the "characteristics" has been corrected, an extra comma (",") has been removed, capitalization of the abbreviation "U.S." has been effected, and a superfluous "and" has been deleted.

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In the paragraph appearing on page 23, beginning at line 12, "IL-4" has been changed to read -- IL-4R --.

In the paragraph appearing on page 25, beginning at line 10, "IL-4R" has been changed to read -- IL-4R --.

In the material appearing on page 27, line 10, "IL-4R (rhuIL-4R)" has been changed to read -- IL-4R (rhuIL-4R) --.

In the paragraph appearing on page 28, beginning at line 24, "IL-4-R" and "IL-4" have each been changed to read -- IL-4R --.

In the paragraph appearing on page 28, beginning at line 31, "IL-4R" has been changed to read -- IL-4R --.

In the paragraph appearing on page 29, beginning at line 9, "IL-4R formulation" has been changed to read -- IL-4R formulations --.

In the paragraph appearing on page 29, beginning at line 16, "IL-4R" has been changed to read -- IL-4R --.

In the paragraph appearing on page 29, beginning at line 23, "formulation" has been changed to read -- formulations --.

In the paragraph appearing on page 30, beginning at line 6, "IL-4R" has been changed to read -- IL-4R --.

In the paragraph on page 31, beginning at line 18, a superfluous beginning parenthesis ["("] has been deleted.

In the paragraph appearing on page 33, beginning at line 6, "ona" has been corrected to read -- on a --.

In the paragraph appearing on page 34, beginning at line 13, capitalization of the abbreviation "ED" has been effected.

In the paragraph appearing on page 35, beginning at line 14, "IL-4" has been changed to read -- IL-4R --.

In the paragraph appearing on page 36, beginning at line 3, a space has been removed between "powder" and "s", and "IL-4" has been changed to read -- IL-4R --.

In the paragraph appearing on page 36, beginning at line 18, "IL-4R" has been changed to read -- IL-4R --, and a comma (",") has been removed following the superscript "4" (both appearances).

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In the paragraph appearing on page 37, line 4, "t oa" has been corrected to read -- to a --.

In the paragraph appearing on page 39, beginning at line 3, "changed" has been corrected to read -- change -- and underlining of "et al." has been removed from the citation of the Maa, Y.F. et al. reference.

In the paragraph appearing on page 40, beginning at line 7, a period (".") has been added.

In the paragraph appearing on page 40, beginning at line 24, "IL-4R" has been changed to read -- IL-4R --.

In the paragraph appearing on page 42, beginning at line 1, capitalization of the word "The" has been effected.

All of the changes to the specification are to correct inadvertent typographical, grammar and/or spelling errors. As the context clearly indicates the intended form, no new matter is introduced by entry of these corrections to the specification.

B. Claims

Claims 1-43 were previously pending in the application. Claims 41-43 have been withdrawn by the Examiner. Claims 1-4 and 6-39 have been amended. No claims have been added or deleted. Consequently, claims 1-40 remain pending and claims 41-43 are withdrawn.

Claim 1 has been amended to read spray-dried particles comprised of interleukin-4 receptor (IL-4R). Support for the change can be found at page 7, lines 1-6. The preambles of claims 1-4, 6-10, and 15-39 have been amended for the sake of consistency among all the claims. Claim 3 has been corrected to remove the superfluous word "either." With respect to adding the words -- in water -- in claims 10-13, support for this addition can be found on page 40, lines 6-25 of the specification. The word "claims" has been changed to -- claim -- in order to provide correct syntax in claim 14. The spelling of the word -- excipients -- has been corrected in claim 22.

As support for the claimed subject matter is found in the application as filed, no new matter is introduced by the entry of the above-identified changes to the claims. The changes to the claims are made for clarification purposes only should not be interpreted as acquiescence in any claim rejection.

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III. The Restriction Requirements

On page 1 of the Office Action, the Examiner maintained the requirement for restriction between Groups I, II and III. The Examiner has withdrawn claims 41-43 from further consideration and indicated that the requirement is final.

Applicants respectfully request reconsideration of the requirements for restriction, based on their arguments filed on February 10, 2004. In addition, Applicants reserve their right to petition the Commissioner to review the requirements for restriction, deferring the filing of the petition until after final action on or allowance of claims, but not later than appeal. See 37 C.F.R. §1.144.

IV. The Rejections Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 1-40 as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Each indefiniteness issued alleged by the Examiner is addressed below.

The Examiner alleged that claim 1 is vague and indefinite for reciting "IL-4R" because the full meaning of the acronym should be stated at its first use in any independent claim. In response, Applicants have provided the meaning of the acronym in claim 1, thereby addressing the Examiner's concern.

The Examiner also alleged that claim 3 is improper because this claim recites "either claim 1" wherein only a single claim 1 exists. In response, Applicants have amended claim 3 to remove the word "either," thereby addressing the Examiner's concern.

The Examiner alleged that recitation of the phrase "spray dried solution or suspension" in claims 4, 6-13, 15-20 and 30-32 is unclear inasmuch as a powder is being claimed. In response, Applicants point out that a powder can be prepared by drying a solution or suspension containing, for example, an active agent such as "IL-4R." Thus, in the case of a "spray dried solution or suspension," a powder can be prepared by "spray drying" an active agent-containing solution or suspension. The powder so prepared can be referred to as the "spray dried solution or suspension." With and/or without regard to this explanation, one having ordinary skill in the pertinent art would understand the meaning of the phrase "spray dried solution or suspension" and how such relates to a powder composition. Thus, based on the foregoing, the Examiner's concern has been addressed.

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The Examiner also alleged that recitation of the term "characterized" renders claims 4, 6-13, 15-20 and 30-32 indefinite because it is unclear whether the limitations following the term are part of the claimed invention. In response, Applicants verify that the element following the term "characterized" in claims 4, 6-13, 15-20 and 30-32 is part of the claimed invention and further defines the invention to which the claim is directed. Thus, based on the foregoing, the Examiner's concern has been addressed.

The Examiner alleged that claim 21 is vague and indefinite because it recites "aerosolized form." In response, Applicants respectfully direct the Examiner's attention to page 6, lines 14-17, wherein the term "aerosolized form" appears. The context of this passage makes clear that a powdered composition can be administered via inhalation when in "aerosolized form." Further, as is made clear by the subject matter encompassed in claim 41, aerosolizing an IL-4R dry powder composition can comprise the step of dispersing the composition into a gas stream. Thus, based on the above, the metes and bounds of the claim are clear and the Examiner's concern has been addressed.

The Examiner also alleged that claim 22 is incorrect because "excipients" has been mis-spelled. In response, Applicants have corrected the error, thereby addressing the Examiner's concern.

The Examiner alleged that recitation of "insoluble aggregates" in claims 10-13 is vague and indefinite because solubility depends on the aqueous media. In response, Applicants have amended these claims to recite a level of insoluble aggregates "in water," thereby addressing the Examiner's concern.

The Examiner also alleged that claim 14 is improper because it recites "claims 1." In response, "claims" has been amended to -- claim -- in order to address the Examiner's concern.

The Examiner also alleged that recitation of the term "emitted dose" in claims 30-32 is vague and indefinite inasmuch as there is no baseline. In response, Applicants respectfully direct the Examiner's attention to the paragraph bridging pages 9 and 10 of the specification where the term "emitted dose" is defined.

Moreover, other patents have issued with claims directed to compositions "characterized by an emitted dose of at least" See, for example, claims 10 and 11 of U.S. Patent No. 6,518,239 to Kuo *et al.* As a patent is presumed to be valid under 35 U.S.C. §282, thereby

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satisfying all the requirements for patentability — including 35 U.S.C. §112 requirements--, it is clear that use of the term "emitted dose" in the claim is neither vague nor indefinite.

The Examiner alleged that claims 2, 5, 25-30 and 37-40 are vague and indefinite insofar as they depend on a claim rejected for reasons of indefiniteness. Having addressed all of the indefiniteness issues raised by the Examiner, Applicants assert that the rejection of these claims should be removed.

Thus, for the above reasons, the Examiner is respectfully requested to reconsider and remove all the rejections under 35 U.S.C. §112, second paragraph.

V. The Rejections Under 35 U.S.C. §102(b)

The Examiner rejected claims 1-32 and 37-40 under 35 U.S.C. §102(b) as being allegedly anticipated by Nossal (1948) *Nature* 162:36-37 ("Nossal"). Ostensibly, the Examiner has taken the position that Nossal discloses each of the elements recited in claims 1-32 and 37-40.

The standard for anticipation is rigorous requiring that every element of the claimed invention be disclosed by a single prior art reference. See *Minnesota Mining & Mfg. Co. v. Johnson & Johnson Orthopaedics, Inc.*, 976 F.2d 1559, 1565 (Fed.Cir.1992); *Scripps*, 927 F.2d at 1576-77; *Lindemann Maschinenfabrik GMBH, v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1458 (Fed.Cir.1984).

Each of the pending claims requires a powder composition comprising spray-dried particles, wherein the spray-dried particles are comprised of IL-4R. In contrast, Nossal teaches an acetone powder composition of erythrocytes, which -- as pointed out by the Examiner -- necessarily comprises IL-4R since IL-4R's are located on erythrocytes. A closer reading of Nossal, however, reveals this teaching relates only to acetone powders. Furthermore, Nossal lacks any description of spray-dried powders, much less of spray-drying techniques that can result in spray-dried powders. Consequently, Nossal does not teach each and every element of the pending claims and the anticipation rejection cannot stand. Reconsideration and removal of the rejection under 35 U.S.C. 102(b) is respectfully requested.

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VI. The First Rejection Under 35 U.S.C. §103(a)

The Examiner has rejected claims 1-40 under 35 U.S.C. §103(a) as being allegedly unpatentable over Mosley *et al.* (U.S. Patent No. 5,599,905) in view of Platz *et al.* (U.S. Patent No. 6,582,728).

In the rejection, the Examiner cites Mosley *et al.* for its teaching of the use of IL-4R in allergy therapy as well as administering IL-4R by bolus injection and other techniques. The Examiner, however, specifically admitted that Mosley *et al.* does not teach the preparation of IL-4R in a powder form.

In an attempt to remedy the deficiency of Mosley *et al.*, the Examiner cites Platz *et al.* for its teaching of using certain powdered compositions for administration by inhalation. The Examiner concludes by asserting that "it would have been *prima facie* obvious to one having ordinary skill in the art to modify the IL-4R polypeptide composition of Mosley *et al.* such that it includes obtaining an IL-4R powder composition as taught by Platz *et al.*" See page 8, lines 16-18, of the Office Action. The Examiner alleges the motivation for doing so lies in the fact that the powdered form (a) is free of liquid propellants, (b) can be easily manufactured, (c) maintains a high percentage of pharmaceutical activity, and (d) exhibits a high level of stability. See the paragraph bridging pages 8 and 9 of the Office Action.

This rejection is respectfully traversed in view of the following remarks.

In order to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *In re Vaack*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Without regard to the other requirements, it is clear the Examiner cannot satisfy the first element, *i.e.*, that there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Thus, assuming *arguendo* it could be shown that there is a reasonable expectation of success and that the prior art reference (or references when combined)

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teach or suggest all the claim limitations, the rejection must nevertheless be withdrawn on the ground that the first element of *prima facie* obviousness has not been satisfied.

None of the reasons provided by the Examiner, however, articulates the requisite suggestion or motivation to modify the cited reference or combine the cited reference teachings. Specifically, the mere fact that the Platz *et al.* may teach a powdered form free of liquid propellants is irrelevant to whether there is a motivation to combine or modify Mosley *et al.*'s teachings; Mosley *et al.* simply fails to disclose the necessity of or desire for alternative formulations, much less alternative formulations that are in powdered form that are also free of liquid propellants. Similarly irrelevant are whether Platz *et al.*'s powders can be easily manufactured, can be made to maintain a high percentage of pharmaceutical activity, or can be shown to exhibit a high level of stability. Thus, rather than articulating the requisite suggestion or motive to modify or combine reference teachings, the Examiner simply sets forth certain advantages believed to be associated with the powders described by Platz *et al.*

Of course, advantages associated with a prior art teaching -- without more -- do not and could not provide the requisite suggestion or motivation to combine or modify any teaching. Because the Examiner simply set forth certain believed advantages of the powders described in Platz *et al.* rather than articulating any suggestion or motivation to modify the reference of combine reference teachings, the Examiner has failed to set forth a *prima facie* case of obviousness.

It is clear that the Examiner did not articulate the requisite suggestion or motivation. A close look at each of the references and an understanding of the knowledge generally available to one of ordinary skill in the art demonstrates why this is so.

With respect to Mosley *et al.*, the reference focuses squarely on IL-4R. As taught in Mosley *et al.* "soluble IL-4 receptor protein can be administered to a patient for treatment." See Mosley *et al.* at column 16, lines 1-3. Furthermore, the reference teaches formulating IL-4R "as a lyophilizate using appropriate excipient solutions (e.g., sucrose) as diluents." See Mosley *et al.* at column 16, lines 19-21. Importantly, there is no hint or suggestion in Mosley *et al.* that speaks to any deficiencies or problems associated with the disclosed IL-4R formulations. As a consequence of there being no disclosed deficiencies or problems associated with the formulations, there is no suggestion and one of ordinary skill in the art would not be motivated to modify the teachings of Mosley *et al.* or combine Mosley *et al.* with another reference, much less combine Mosley *et al.* with the specific reference of Platz *et al.* as is urged by the Examiner.

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Turning to Platz *et al.*, this reference focuses on dispersible dry powders. As understood by the Examiner, the described powders have many advantages such as not requiring propellants and ease of manufacture. Such advantages -- without more -- is insufficient to set forth a *prima facie* case of obviousness.

Finally, the knowledge of one of ordinary skill in the art would likely not provide the necessary suggestion or motivation. For example, in order to arrive at the claimed invention, one would first have to focus on solid formulations yet ignore Mosley *et al.*'s teaching of a lyophilized form. Then, among all possible solid forms one would need to concentrate on particulate solid forms. Of the many types of particulate forms, one would then have to focus on particulate forms that are prepared by spray drying. Then, among the spray drying teachings, one of ordinary skill in the art would then need to somehow choose Platz *et al.* There simply is no basis to believe that one of ordinary skill in the art would be led to take these steps.

Clearly, the suggestion to modify the references to reach the claimed invention comes only from the Examiner after reading the blueprint provided by Applicants' specification. This approach is consistently criticized as impermissible "hindsight reconstruction" and cannot be relied upon in the formation of a *prima facie* case of obviousness.

Moreover, assuming *arguendo* that the Examiner could somehow establish that the teachings of the cited references *could* be combined or modified, such a showing would nevertheless be insufficient. As pointed out in Section 2143.01 of the Manual of Patent Examination and Procedure ("M.P.E.P."),

[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). ... Although a prior art device "may be capable of being modified to run the way the apparatus is claimed, there must be a suggestion or motivation in the reference to do so." 916 F.2d at 682, 16 USPQ2d at 1432.). See also *In re Fritch*, 972 F.2d 1260, 23 USPQ2d 1780 (Fed. Cir. 1992) (flexible landscape edging device which is conformable to a ground surface of varying slope not suggested by combination of prior art references). [Emphasis in original.]

Thus, even if Mosley *et al.* and Platz *et al.* could be combined and a successful outcome achieved technically, the standard of *prima facie* obvious still requires that there be some suggestion or motivation, either in the references themselves or in the knowledge generally

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available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. As pointed out above, such suggestion or motivation simply does not exist.

In sum, by being able to provide any suggestion or motivation to modify the reference of combine reference teachings, the Examiner has failed to set forth a *prima facie* case of obviousness. Moreover, even if the Examiner somehow demonstrated that the references *could* be combined, such a showing is irrelevant as the Examiner must nevertheless show the required suggestion or motivation. As a result, the obviousness rejection of claims 1-40 under 35 U.S.C. §103(a) is unsustainable for at least the above reasons. Reconsideration and withdrawal of the rejection is respectfully requested.

VII. The Second Rejection Under 35 U.S.C. §103(a)

The Examiner has rejected claims 1-40 under 35 U.S.C. §103(a) as being allegedly unpatentable over Lange (1999) *Cardiovascular, Pulmonary and Renal Investigational Drugs* 1(4): 526-531 ("Lange") in view of Platz *et al.* (U.S. Patent No. 6,582,728).

Lange has been cited as teaching administration of IL-4R for the treatment of individuals suffering from asthma, wherein IL-4R is administered as a spray in solution form. Lange has also been cited as teaching administration of IL-4R in a single dose. The Examiner admits that Lange does not teach the preparation of IL-4R as a powder form. See page 9, lines 10-12, of the Office Action. With respect to Platz *et al.*, this reference has been previously discussed in Section VI, above.

This rejection is respectfully traversed in view of the following remarks.

The three criteria for establishing a *prima facie* case of obviousness have been set forth in Section VI, above.

Again, it is clear that the Examiner cannot satisfy the first element of *prima facie* obviousness, i.e., there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings.

Lange does little, if anything, to correct the deficiencies of the *prima facie* obviousness set forth above. For example, when compared to Mosley *et al.*, the reference merely teaches inhalation by asthma patients of IL-4R as a spray. Importantly Lange teaches that "[i]n light of the mild side effects and ease of administration associated with Nuvance [i.e., soluble human

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IL-4R administered by inhalation via a spray], the successful development and rapid acceptance of this biological is likely." In addition, Lange does *not* teach that there is any significant disadvantage or problem with administering IL-4R via a spray such that there is a suggestion or motivation to modify the reference or combine the reference with another.

Thus, inasmuch as Lange does little, if anything, to correct the deficiencies of Mosley *et al.*, the second rejection under 35 U.S.C. §103(a) suffers from the same infirmities identified above in Section VI with respect to the first rejection. As a consequence, the second obviousness rejection of claims 1-40 under 35 U.S.C. §103(a) is unsustainable for at least the reasons provided here and above in Section VI. Reconsideration and withdrawal of the rejection is respectfully requested.

VIII. Conclusion

In view of the foregoing, Applicants submit that the pending claims satisfy the requirements of patentability and are therefore in condition for allowance. Reconsideration and withdrawal of all objections and rejections is respectfully requested and a prompt mailing of a Notice of Allowance is earnestly solicited.

If a telephone conference would expedite the prosecution of the subject application, the Examiner is requested to call the undersigned at (650) 620-5506.

Respectfully submitted,
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Date: September 21, 2004

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